

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

Applicant's or agent's file reference MJPah-F0598/62WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/00448	International filing date (day/month/year) 08.01.2003	Priority date (day/month/year) 08.01.2002
International Patent Classification (IPC) or both national classification and IPC C07K14/575		
Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA ... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.
 - This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
 - I Basis of the opinion
 - II Priority
 - III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV Lack of unity of invention
 - V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI Certain documents cited
 - VII Certain defects in the international application
 - VIII Certain observations on the international application

Date of submission of the demand 03.07.2003	Date of completion of this report 26.04.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stolz, B Telephone No. +49 89 2399-8416



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/00448

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-23 as originally filed

Claims, Numbers

1-12 as originally filed

Drawings, Sheets

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/00448

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-12
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-12

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/00448

1. The application discloses prolactin receptor antagonists with antiproliferative activity consisting of N-terminally modified/truncated hPRL with a sterically hindering mutation in the second binding site.
2. The subject matter of claims 1 to 12 has not been disclosed in the prior art.
3. The subject matter of claims 1 to 12 lacks an inventive step in view of Bernichein et al. in combination with Goffin et al..

Bernichein et al. provides a preliminary account of studies on the effect of N-terminal deletions on the activity and multimerization of hPRL. The aim of their study is the design of more potent hPRL antagonists. The abstract discloses an effect of the removal of the N-terminal loop on the tendency to multimerize. The abstract explicitly suggests the combination of N-terminally deleted hPRL with site 2 analogs such as disclosed in Goffin et al., in order to obtain more potent hPRL antagonists.

Following the explicit teaching of Bernichein et al., i.e. by combining the two types of mutations, the person of skill would have found himself in a one way street situation. He would have tested the molecules by the methods known in the art and would unavoidably have found PRL antagonists having lost their agonistic activity.

Therefore, the claims are considered to lack an inventive step.

PATENT COOPERATION TREATY

PCT

**NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT**

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

VIALLE-PRESLES, Marie José
 CABINET ORES
 36, rue de St-Petersbourg
 F-75008 PARIS
 France

CABINET ORES

19. MAI 2003

Date of mailing (day/month/year) 29 April 2003 (29.04.03)			
Applicant's or agent's file reference MJPbv598/62	IMPORTANT NOTIFICATION		
International application No. PCT/EP03/00448	International filing date (day/month/year) 08 January 2003 (08.01.03)		
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 08 January 2002 (08.01.02)		
Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - INSERM et al			

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed to Rule 17.1(c)** which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed to Rule 17.1(c)** which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
08 Janu 2002 (08.01.02)	02290030.2	EP	23 Apri 2003 (23.04.03)

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.89.70

Authorized officer

Khemais BRAHMI (Fax 338 8970)

Telephone No. (41-22) 338 9715

PCT**NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

VIALLE-PRESLES, Marie José
 CABINET ORES
 36, rue de St-Pétersbourg
 F-75008 PARIS
 FRANCE

CABINET ORES

28. JUIL 2003

Date of mailing(day/month/year) 17 July 2003 (17.07.03)
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Applicant's or agent's file reference MJPbv598/62
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International application No. PCT/EP03/00448	International filing date(day/month/year) 08 January 2003 (08.01.03)	Priority date(day/month/year) 08 January 2002 (08.01.02)
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Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - INSERM	IMPORTANT NOTICE
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1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:

CH, EP, KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OA, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 17 July 2003 (17.07.03) under No. 03/057729

4. TIME LIMITS for filing a demand for international preliminary examination and for entry into the national phase

The applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be 30 MONTHS from the priority date, not only in respect of any elected Office if a demand for international preliminary examination is filed before the expiration of 19 months from the priority date, but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see *PCT Gazette* No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the *PCT Newsletter*, October and November 2001 and February 2002 issues.

In practice, time limits other than the 30-month time limit will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For regular updates on the applicable time limits (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

For filing a demand for international preliminary examination, see the *PCT Applicant's Guide*, Volume I/A, Chapter IX. Only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

It is the applicant's sole responsibility to monitor all these time limits.

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Authorized officer

Judith Zahra

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